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An Evaluation of Research on

Lymphoid Leukosis And Marek's Disease

Agricultural Research Service

United States Department of Agriculture

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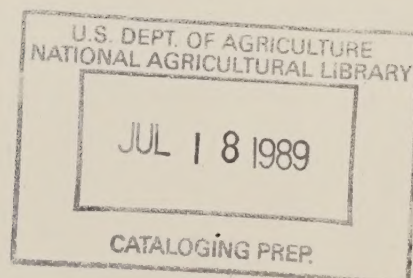


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**An Evaluation of Research
on Lymphoid Leukosis
and
Marek's Disease**

June 1975

**United States Department of Agriculture
Agricultural Research Service**



Summary

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Research by the Agricultural Research Service (ARS) on lymphoid leukosis and Marek's disease has been conducted since 1939 at the Regional Poultry Research Laboratory, East Lansing, Michigan, and concurrently at the Animal Physiology and Genetics Institute, Beltsville, Maryland, since 1967. As of July 1975, all research will be conducted in East Lansing.

As a direct result of ARS research, the causative virus of lymphoid leukosis was isolated and genetic resistance in chickens to this disease was shown. In 1967, the causative virus of Marek's disease was isolated, and in 1969, a herpesvirus isolated from turkeys (HVT) was shown to protect chickens against Marek's disease. Laboratory and field trials of the HVT vaccine were completed in 1970, and the vaccine was licensed for national use in 1971.

The cost of the research on lymphoid leukosis and Marek's disease to ARS was \$6 million before 1965 and \$9 million from 1966 to 1975. The total cost of the research, including ARS, CSRS, other federal and state funds, was \$31 million. In 1974, the last full year, the cost was \$2.16 million.

Benefits from the use of the herpesvirus of turkeys vaccine against Marek's disease included \$91 million reduction in broiler condemnations, a \$10 million reduction in broiler mortality, a \$10 million reduction in feed necessary to produce broilers and a \$17 million reduction in broiler breeder mortality. In egg-type chickens, benefits from the vaccine included a \$67 million reduction in chicken mortality and a \$350 million increase in egg production. The biologics industry benefited by \$13 million. There was also a benefit of \$58 million from decrease in lymphoid leukosis due to increasing the genetic resistance of commercial chickens to this disease. Other benefits include contribution to the knowledge of human cancer and a significant impact of the ARS research on other research in similar related fields.

By any measure, the investment in research on lymphoid leukosis and Marek's disease has paid off handsomely. Thus, the overall benefit was \$616 million; the benefit in 1974 alone was \$180 million. The benefit was derived from increased efficiency in broiler and egg production, which thus conserved feed and saved labor and capital. Some of the benefits were to the poultry and biologics industries, but the greatest benefit was to the consumer in the form of a more uniform, less expensive product than would have been available had the technology not been developed.

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Table of Contents

Introduction.....	1
Historical Perspective.....	1
History.....	1
Disease Nomenclature.....	2
Location of Work.....	2
Objective of Research.....	3
Missions and Goals.....	3
Technological Objectives.....	3
Cost of Research Program.....	4
Research Discoveries and Implementation of Results.....	5
Contribution of ARS Research to Objectives.....	5
Research Discoveries in Marek's Disease.....	6
Research Discoveries in Lymphoid Leukosis.....	7
Implementation of Results.....	8
Benefit from Research Program.....	8
Estimation of Losses from LL and MD.....	8
Benefits from the Control of MD in Poultry.....	9
Benefits from Studies on LL.....	13
Benefits for Human Cancer.....	14
Impact of Research on the Field of Science.....	14
Summation.....	16
Future Direction of Research.....	16
Figures.....	18
Tables.....	20
Appendix 1 References.....	
Appendix 2 Publications.....	
Appendix 3 Honors and awards.....	

Introduction

Departments and agencies of government are funded to carry out specified operations and functions judged to be in the public interest. The effectiveness and efficiency with which such missions are discharged are a legitimate concern of the public and their selected and appointed representatives. The President's Office of Management and Budget has directed that federal departments and agencies provide for continuing systematic review of all aspects of program management, including the evaluation of program effectiveness in accomplishing program objectives.

The Department of Agriculture has established a Program Evaluation System administered in the Office of Planning and Evaluation to assure that such evaluation is carried out. In its guidelines to the agencies, Office of Planning and Evaluation has defined program evaluation as the ex post facto evaluation of the effectiveness of ongoing programs in meeting the goals of USDA missions, achieving program objectives, and serving specified target groups. The purpose of this paper is to report the evaluation of a definable segment of ongoing Agricultural Research Service research, that on lymphoid leukosis and Marek's disease of poultry.

Historical Perspective

History

Mortality among laying chickens became a very pressing problem in commercial flocks throughout the United States from 1925 to 1937. This was a period when there was a very rapid growth in the commercial poultry industry. A large part of the mortality was attributed to one or more of the diseases included in what was later referred to as "the avian leukosis complex" (see section on Disease Nomenclature). In 1937, through the efforts of representatives of practically every segment of the poultry industry, poultry scientists and experiment station directors of the north central and northeastern states, the Regional Poultry Research Laboratory (hereafter referred to as the RPRL) was established. This laboratory was established under the Bankhead-Jones Act of 1935 which provided for the establishment of regional laboratories for special research administered by the Secretary of Agriculture in cooperation with the state experiment stations. The original building was dedicated on August 8, 1939.

The regional nature of the laboratory and its activity was further emphasized by the signing of a memorandum of agreement between the U.S. Department of Agriculture and 25 state agricultural experiment stations. Because of the special requirement for research within this disease complex, active participation by many of these experiment stations became gradually reduced until by World War II only a few experiment stations were actually working on the disease. The effort is currently almost entirely in the hands of this laboratory in the United States and the Houghton Poultry Research Station, Houghton, England.

Disease Nomenclature

In the 1920's and the 1930's, at the time the RPRL was established, "leukosis" was considered to be a neoplastic disease (cancer) of unknown etiology.

In the 1940's and 1950's the "avian leukosis complex" was thought to be caused by a single group of viruses and included neural, visceral, and ocular lymphomatosis. Genetic resistance to these diseases was recognized.

By the 1960's, the "avian leukosis complex" was recognized as two diseases: (a) lymphoid leukosis (LL) and its related tumors caused by groups of RNA tumor viruses, and (b) Marek's disease (MD) caused by DNA tumor viruses. (RNA viruses contain as their genetic material ribonucleic acid and DNA viruses contain deoxyribonucleic acid).

Now three groups of viruses are recognized, (a) and (b) above and the reticuloendotheliosis group of RNA viruses. Because of the similarity of lesions produced by these three groups of viruses, they are difficult to distinguish on a routine basis. Thus, the Animal and Plant Health Inspection Service, whose inspectors examine most poultry slaughtered for human consumption, condemn poultry carcasses showing any lesions of "leukosis." In broilers and young chickens this condemnation is entirely due to MD. In mature chickens condemnation is due to a mixture of LL and MD, but probably mostly the former. Reticuloendotheliosis occurs very rarely in poultry. Most of the research performed from 1965 to 1975 at the RPRL concerned MD. The herpesvirus of turkeys (hereafter referred to as HVT) vaccine was developed during this period and prevents mortality from MD and condemnations among young chickens from "leukosis."

Location of Work

By the early 1960's, workers recognized that the high rates of mortality and condemnations in the industry were largely due to MD, but the RPRL had worked largely on the causative agents of LL. In 1965 and 1966 the research here shifted almost entirely to that concerning MD, but it was recognized that mortality from LL remained a problem.

In 1967 work on genetic resistance to LL was moved to the Agricultural Research Center at Beltsville, Maryland, where it became part of the Genetics Investigations of the Poultry Research Branch and later part of the Avian Physiology Laboratory of the Animal Physiology and Genetics Institute. This phase of the work has continued at Beltsville in coordination with the RPRL until 1975.

By 1972 the HVT was in use as a commercial vaccine and part of the effort at the RPRL was shifted back to LL.

Later this year (1975), the Beltsville unit will move back to the RPRL to provide a better coordinated and balanced research program on the neoplastic diseases of poultry.

Objective of Research

Missions and Goals

Of the 11 missions describing the Department's role in solving broad national problems, the research under evaluation falls in the mission of "Agricultural Production and Marketing Efficiency." The USDA missions are currently defined in terms of 39 goals and 247 programs that contribute to the achievement of these goals. The research under evaluation falls under operating goal No. 2, "New Knowledge to Increase Productivity," and Program No. 678, "Animal Production Efficiency Research." The objectives of this program are to develop knowledge that will enable farmers to produce abundant dairy, meat, poultry, and other animal products at low cost to the consumer while obtaining desirable return on their investments through the use of (a) improved genetic characteristics; (b) improved reproduction efficiency; (c) greater control and prevention of disease, insects and other pests; (d) improved feeding and management practices; and (e) improved machinery, buildings, equipment, energy use efficiency, and related inputs.

Control of lymphoid leukosis (LL) and Marek's disease (MD) are under the objective of prevention of disease in poultry. With healthier and more productive animals, loss from disease will decrease and production efficiency will improve. Thus, the research clearly relates to the program, goal, and mission of the USDA of improving agricultural production efficiency, of which improving poultry efficiency is a part. With improved efficiency, food production in the world can be substantially increased. The increased food production is one approach to decreasing hunger in the world. Also, (36) "food can become an instrument of peace in international diplomacy." Thus, reduced losses in poultry from LL and MD are a small part in the attempt to reduce world hunger and maintain peace on earth.

This research is classified in the Current Research Information System under Research Problem Area 211 - Control of Diseases of Livestock, Poultry, and Other Animals.

Technological Objectives

The objectives of the research under evaluation were to reduce losses in poultry from mortality, morbidity, reduced egg production and condemnation after slaughter due to LL and MD.

The research program at the time the Regional Poultry Research Laboratory was started was in the areas of genetics, pathology, management, and nutrition. Genetics research included research to develop lines of chickens inherently resistant and susceptible to disease; to produce lines of chickens free of, yet highly susceptible to, the disease; and to determine whether the disease is transmitted from parent to offspring through hatching eggs. Pathology research included studies of the causative agent or agents and the methods of transmission, the passage and the maintenance of the agent(s), the gross

and microscopic study of diseased chickens, and a study of the physical and biological properties of the causative agent(s). Other research included the influence of environmental and nutritional factors, and of sex hormones and sex organs upon disease. Development of tests used in the diagnosis of the disease were pursued jointly with the Michigan State Agricultural Experiment Station with the financial assistance of the National Cancer Institute of the U.S. Public Health Service, Bethesda, Maryland.

In 1961 the research program was expanded to include the following: (a) breeding chickens for further genetic resistance or susceptibility; (b) determining the mode of inheritance of resistance; (c) developing and maintaining, for use in critical research, inbred lines of chickens that are not only highly susceptible but are free of leukosis and other diseases; (d) determining the biological and physical characteristics of the virus or viruses causing these diseases; (e) studying the pathology, immunology, and serology of the diseases to acquire a complete knowledge of host-response to infection; (f) developing methods, products, and instruments for the specific detection and assay of the tumor-producing agents and biologic reaction to these methods and procedures; (g) conducting epidemiological research for the purpose of contributing to a complete understanding of the diseases and developing measures for limiting the spread of infection; (h) developing methods, procedures, and agents for the control of these diseases; and (i) determining the effect of feeding certain nutrients on the incidence of visceral lymphomatosis. Although the emphasis on different areas has changed over the years, the USDA research program today remains essentially the same.

Cost of Research Program

The Agricultural Research Service (ARS) budget for research on lymphoid leukosis and Marek's disease was \$8.555 million for the fiscal years 1966 to 1975 with an additional \$0.572 million for extramural research (Table 1). In addition, \$0.45 million was appropriated in 1962 for construction of a new laboratory which was completed in June 1973. The entire ARS budget for this research prior to 1966 was \$5.93 million. Thus, in the 36 years ending June 1975, approximately \$15.06 million was spent on ARS research on lymphoid leukosis and Marek's disease (Tables 1 and 19).

Expenditures for the 10 fiscal years 1966 to 1975 by the Cooperative States Research Service, Federal agencies other than USDA and state institutions are also listed in Table 1. The total support from all sources for the research amounted to \$18.538 million for the 10 years 1966 to 1975. Expenditures from 1939, when the Regional Poultry Research Laboratory was established, to 1965 are estimated to be \$5.93 million. This represents approximately 65% of the expenditure from 1966 to 1975. Assuming other sources expended a similar proportion, their expenditure for 1965 and earlier would be \$6.11 million. When added to the budget for Cooperative States Research Service which was \$2.20 million, to the budget for the states which

was \$6.27 million, and to the other Federal expenditures which was \$0.94 million, the total cost of the research was \$30.58 million.

The total scientific man-years in ARS from 1966 to 1975 were 98 and for the state agricultural experiment stations 184 (Table 1).

Research Discoveries and Implementation of Results

Contribution of ARS Research to Objectives

Because of the great problem caused by lymphoid leukosis (LL) and Marek's disease (MD), many public and private institutions had small research programs to control these diseases. Also, involved was a large group of scientists interested in the causation and cure of human cancer.

Research organizations making significant contributions to the control of Marek's disease included the Regional Poultry Research Laboratory (RPRL), East Lansing, Michigan; the Houghton Poultry Research Station, Houghton, England; the Southeast Poultry Research Laboratory, Athens, Georgia; the University of Massachusetts, Amherst, Massachusetts; and Cornell University, Ithaca, New York. There was often close cooperation between the staffs at these institutions, and discoveries by one group were soon corroborated in other laboratories. The important events that led up to the development and use of the herpesvirus of turkeys (HVT) against MD are listed in Table 2. Contributions made by the ARS scientists are underlined. All are from the RPRL, East Lansing, Michigan. Separating the contribution of ARS scientists from those of other scientists is difficult. However, the major contributions of ARS scientists were in the discovery of the causative MD virus, the discovery of the HVT, the demonstration that HVT would protect against MD, and the laboratory and field trials that led to licensing of the vaccine for national use. Because all the major discoveries were made by ARS scientists and because the contribution of other groups was small and mainly in maintaining a level of competition, all the benefits from the HVT vaccine against MD are considered due to the discoveries by ARS scientists.

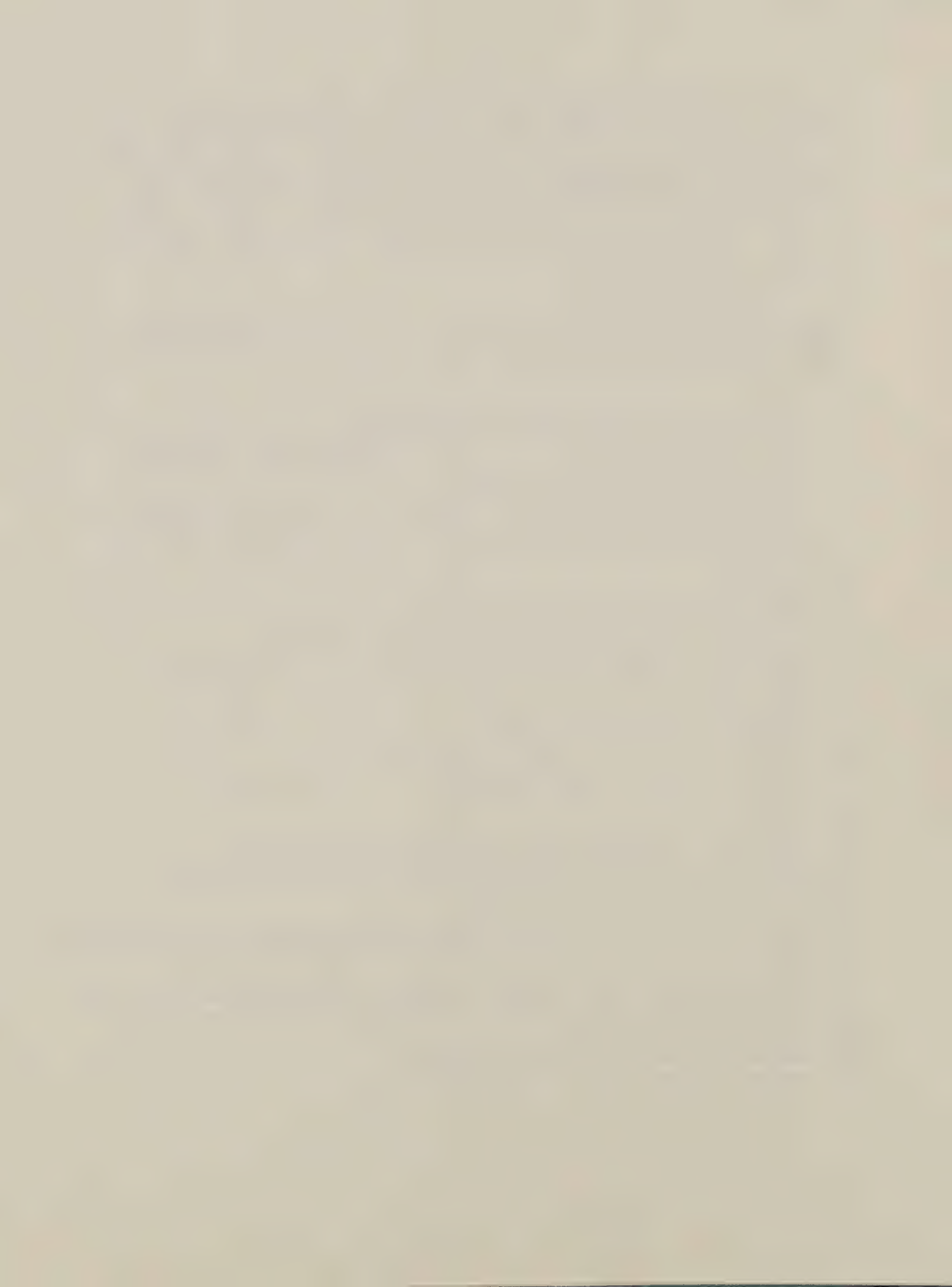
In LL research the laboratories mainly involved were the RPRL; the Animal Physiology and Genetics Institute, Beltsville, Maryland; and the Houghton Poultry Research Station, Houghton, England. A few members of the National Cancer Institute, National Institutes of Health, Bethesda, Maryland, were also involved in this research. In more recent years, some universities have become involved. The major pioneering discoveries from 1939 to 1965 were made by ARS scientists. These discoveries include the demonstration of the viral etiology of LL, the role of egg transmission in the disease, the identification of field strains of virus pathogenic for chickens and the demonstration that resistance of the chicken to infection by the virus was due to a single gene. In subsequent years, from 1965 to 1975, some discoveries have been made solely by ARS scientists, e.g., the two levels of genetic resistance to LL and the pathogenicity of different subgroups of virus including endogenous virus. Other discoveries have been made in cooperation with state and other federal institutions, e.g., the role of the bursa of Fabricius in the pathogenesis of disease and the association of certain types of resistance with blood type. Still other discoveries have

been made by institutions supported by funds for human health; e.g., methods for assay of leukosis viruses, mutants of leukosis viruses, and studies of the nucleic acid of these viruses. Most of the contributions of ARS scientists have been directed toward resolving the LL problem in the poultry industry whereas contributions of scientists in the human health field were directed toward the basic causation of cancer. Thus, at least one-half of the benefits to the poultry industry from lymphoid leukosis research can be considered due to discoveries by ARS scientists.

Research Discoveries in Marek's Disease

The following list includes discoveries by ARS staff at the RPRL from 1965 to 1975. Each discovery was of significant information necessary before certain subsequent discoveries could be made.

1. Isolation of the causative herpesvirus of MD.
2. Development and standardization of methods for assay of the virus.
3. Development and production of a line of chickens highly susceptible to MD. Susceptible chickens are required for in vivo assay, vaccine challenge and pathogenesis studies.
4. Microscopic and ultrastructural changes of cells and cell cultures resulting from infection with the virus. Recognition of these changes is required for the in vitro assay of vaccine potency and many other studies.
5. Application of immunofluorescent technique for the detection and assay of MD virus (MDV) antigen and antibody.
6. Discovery of virus production in the feather follicle.
7. Detection, assay and production of cell-free MDV and HVT.
8. Application of neutralization test and assessment of neutralizing antibodies.
9. Verification and study of essential parameters of the agar gel precipitin test of MDV antibody.
10. Attenuation of MDV and study of properties.
11. Studies in depth of the epizootiology of MD including spread between chickens and persistence in chickens.
12. Isolation of HVT.
13. Comparative antigenic studies of MDV and HVT.
14. Detection of surface antigens in cells infected with MDV.
15. Comparative study of the pathogenicity and antigenicity of virus clones from strains of MDV and HVT.
16. Absence of egg transmission of MDV.
17. Laboratory protection and safety tests of HVT in chickens and in humans.
18. Effect of vaccination with HVT on the horizontal spread of MDV.
19. Large scale production of MDV.
20. Susceptibility of cell cultures of various avian species to MDV and HVT.
21. Temporal relations between HVT vaccination and challenge with MDV.
22. Storage of HVT vaccine.
23. Lack of oncogenicity of HVT for turkeys.
24. Mechanism of protection of HVT against MD.



Research Discoveries in Lymphoid Leukosis

The following list includes discoveries made from the time the RPRL was established until now (1975). They include those made by scientists at the Animal Physiology and Genetics Institute, Beltsville, Maryland. The discoveries made by ARS scientists are indicated by (ARS).

1. Recognition of LL as a viral disease (ARS).
2. Demonstration of egg transmission of the LL virus (LLV) (ARS).
3. Demonstration of contact transmission of the virus (ARS).
4. Development of cell culture assay systems for the LLV (Univ. of Calif.).
5. Identification of single genes controlling cellular resistance to LLV infection (ARS).
6. Demonstration that "field" strains and "laboratory" strains of LLV are similar agents (ARS).
7. Recognition of the close association of LL viruses with sarcoma viruses (ARS, Univ. of Calif.).
8. Recognition of the group-specific antigen of the LLV, and development of the complement fixation for avian leukosis viruses (COFAL) test (National Institutes of Health).
9. Recognition that genetic resistance to LL can be aimed at resistance to virus infection or at tumor development (ARS).
10. Classification of LLV into subgroups (Univ. of Calif.).
11. Demonstration that genetic cellular resistance reduces the incidence of neutralizing antibody and disease (ARS).
12. Identification of the bursa of Fabricius as the target organ for the initial lymphoid tumor transformation (ARS, Univ. of Minn.).
13. Demonstration of single genes for resistance, each of which are specific for a different subgroup of LLV's (ARS, England).
14. Identification of a single dominant gene controlling the expression of LLV group-specific antigen in the absence of virus (England).
15. Development of the non-producing cell test for LLV (ARS).
16. Demonstration that a single gene for virus resistance is associated with a blood group gene (ARS).
17. Recognition of the spontaneous production of the endogenous LLV (RAV-0) (Univ. of Calif.).
18. Demonstration of high-frequency recombination in the leukosis-sarcoma group of viruses, leading to studies of virus genetics and understanding of viral functions (Univ. of Wash. & Public Health Research Institute, New York).
19. Identification of dominant genes controlling spontaneous RAV-0 production (ARS).
20. Demonstration that all subgroups of LLV tested induce LL except the viruses related to the endogenous LLV (RAV-0). This discovery indicates that the control of endogenous virus is not important to the poultry industry (ARS).
21. Development of the phenotypic mixing test for assay of LLV's (ARS).

Implementation of Results

The time between the development of the HVT vaccine against Marek's disease as a commercially applicable vaccine and its adoption by 95% of the industry was 2 years (36), a time much shorter than that required to adopt many other agricultural discoveries, some of which have required one or more decades (Table 3). Also, the time between the discovery of HVT and the licensing of it as a vaccine was approximately 2 years, an exceptionally short time to demonstrate safety and efficacy for commercial use. The speed with which commercial companies obtained approval to use the vaccine and the speed of adoption was due in large part to the extent and thoroughness of the research at the RPRL. Without these experimental results, the time needed for licensing and adoption would have been much longer.

The causative agent of LL was discovered in the early 1950's and a cell culture test for detection of the virus was discovered in the 1960's. These discoveries led directly to the requirement by Federal regulatory agencies that all vaccines for human and animal use that are grown in chicken eggs be free of LLV's. A number of lines of LLV-free chickens whose eggs are used for vaccine production and research purposes have been developed. At least three large breeders of egg-type chickens have progressed or are progressing towards making their basic lines free of these viruses. However, the technology has not been universally adopted, mainly because of the high cost of testing, the disruption of the breeding programs required for development of LLV-free flocks, and the lack of knowledge of the importance of LL to the commercial industry. Some progress has been made in breeding chickens for genetic resistance. The time between the discovery of genetic resistance in chickens and its implementation by some breeders was about 7 years. This implementation never attained wide acceptance because breeders were generally unwilling to add another trait to their breeding objectives. Breeding for genetic resistance to LL is continuing in some companies.

Benefit from Research Program

Estimation of Losses from LL and MD.

Actual losses from LL and MD for 1965 are listed in Table 4. The losses from MD condemnation visualized for 1975, had new technology not been applied, are average losses prevailing just prior to beginning use of the vaccine in 1971. Thus, in the case of condemnation of broilers from MD, losses rose consistently each year from 0.5% in 1965 to a maximum of almost 1.6% in 1970 (Table 5). In view of the fact that condemnations had been increasing each year and would likely have continued to increase after 1970, we have assumed that, as a minimum, condemnations would have remained at least at the 1970 level for the years 1970 to 1975; i.e., 1.6%, had new technology for the prevention of the disease not been introduced. This national average is lower than the losses in Georgia, where losses reached a maximum of 2.89% (Table 5). Layer mortality from LL declined from 5.0% in 1965 to 4.0% in

1975 due to improved genetic resistance to LL. All other factors listed under old technology in Table 4 were considered unchanged between 1965 and visualized 1975 losses.

The losses under actual new technology for 1975 are the most recent data available. For broiler condemnation and for condemnation from other causes, the data represent the actual figures for 1974. Data for broiler mortality were estimated from 1975 statistical estimates. The losses under 1975 actual technology for the other items listed in Table 4 are derived from the best estimates available from national statistics, field trials, or laboratory trials, in the order of preference where available.

The losses under the visualized new technology in 1985 are comprised of 30 to 60% of the actual losses for 1975 from MD and of 20 to 90% of the losses from LL. Most of the improvement between the actual losses in 1975 and the visualized losses in 1985 are from improvement in the HVT vaccine and its complete adoption by the industry, together with a reduction in the total level of MD virus in the poultry population. In egg-type chickens the reduction between 1975 actual losses and 1985 visualized losses is mainly due to the development of control measures for LL.

Benefits from the Control of MD in Poultry

The following general method was used to estimate the benefit from vaccination. First, the proportion of the product saved each year by vaccination was estimated from national figures or from laboratory and field experiments. The value of this part of the product for each year was then estimated from the annual gross value of the product in the United States. The gross value of the product was from published statistics. The value of the product saved in the first half of 1975 was assumed to be half the value of the product for 1974.

When the proportion of product saved is applied to the total value, the cost of chicks, vaccine, feed, labor, farm capital, processing and marketing of the saved product is taken into account. The effect of the technology on the price of the product is also taken into account. Other factors that affect the price may inadvertently be included; e.g., other diseases such as the exotic Newcastle disease outbreak and variations in demand. However, the benefits are estimated in terms of the average market conditions operating during that year. The benefits are, therefore, an estimate of the change in cost of production and reflect the increased production efficiency.

Because the vaccine is applied when chicks are 1 day of age and broilers are marketed at 8 weeks and eggs between 20 and 80 weeks thereafter, there is a delay between expenditures and reaping the rewards of vaccination. But broiler and egg production are year-round operations with only minor seasonal fluctuations in quantity and value, so this lag would have minimal effect on the value of benefits obtained from vaccination.

1. Broiler Condemnations from MD

Loss due to condemnations from "leukosis," which, in fact, was loss from MD, was 1.57% of chickens slaughtered in 1970 (33), the last year of statistics before the vaccine was used extensively in the field. Assuming, as explained earlier, that condemnations would not decline, but allowing for some uncertainty in the estimate of condemnation rate, we assumed that the condemnations would have continued in the years from 1971 to 1975 at a rate 90% of that in 1970, i.e., 1.41%, had the vaccine not been developed. Reduction below this level is considered to be due to the control of MD by the HVT vaccine (Table 6). The loss due to the condemned chickens was taken as the total of the fair market value because the salvage value from rendering the condemned birds is very small. Results of applying the procedure described above are shown for each year since 1970 (Table 6). It is apparent that, under the assumptions made, application of the vaccine has reduced losses from condemnations by \$75.35 million.

2. Broiler Condemnations from Causes other than MD

MD weakens chickens so that they become more susceptible to other diseases. In one laboratory experiment, 18 of 26 (69%) unvaccinated, MD-infected chickens responded immunologically to Mycoplasma synoviae with a mean HI titer of 46.9; whereas, 24 of 24 (100%) of the vaccinated chickens responded with a titer of 67.6 (15). A similar effect was noted with coccidiosis; i.e., MD-infected birds were more susceptible to two strains of coccidiosis, shed more oocysts and developed a poorer immunity to subsequent rechallenge than birds without MD infection (1). Vaccination with an attenuated MDV vaccine against MD decreased mortality from causes other than MD from about 20% to 12% (2). Much of this mortality was coccidiosis. Mortality from causes other than MD was reduced by the vaccination from 17.2 to 15.9% (23). In field trials, condemnations from causes other than MD were reduced by vaccination with HVT from 0.59% to 0.25% (8). Also, national condemnations from causes other than leukosis decreased after 1970 when vaccination was introduced. Husbandry and other factors had very little to do with this reduction, and the major part was due to the HVT vaccine, which resulted in healthier chickens more able to resist other diseases. A conservative estimate of the role of vaccine is that 50% of the reductions in condemnations from causes other than MD were from the effect of the vaccine.

Methods similar to those used to calculate benefits from condemnations from MD above, were used to calculate benefits from condemnations from causes other than MD; these benefits were \$15.13 million (Table 7).

3. Broiler Mortality

In a similar manner a part of the total broiler mortality is considered to be due to MD and is reduced by vaccination. In one trial, mortality among 2.5 to 5 thousand broilers was reduced from 3.3 to 2.3% in 3 to 9 weeks (8). In another trial, livability among 2.5 million birds was increased 1.8% by vaccination (9). Because the effects of MD are late in the broiler's life, but considerable broiler mortality may occur before 3 weeks, only 10% of the reduction in mortality was considered to be vaccine related. This figure is

conservative when compared with the above figures. Also, because mortality from MD is late, the broilers would have to be fed for almost the entire 9 weeks so that the value of the chickens that died can be considered the same as those marketed.

The mortality of broilers was obtained by subtracting the number sold at 8 weeks from the number hatched (Table 8) for 23 states for which the Statistical Reporting Service collects statistics. Figures including all states are slightly higher but include home consumption and therefore were not used. The resulting mortality varies considerably from year to year. The vaccine was not in general use in broilers until later than in egg-type chickens and the effects on condemnations of broilers (Table 6 and 7) were not noticeable until 1972. Thus, the average mortality prevailing just prior to beginning use of the vaccine was taken as the average for the years from 1969 to 1971 rather than the figure for 1970 which appeared to be unusually low. Total benefits from vaccination on mortality are \$9.7 million (Table 8).

4. Feed Conversion in Broilers

Eidson et al (9) estimate, on the basis of trials involving approximately 3 million chickens, that vaccination of broilers with one-half dose or less of vaccine has increased body weight of vaccinated birds 0.1 pounds and that vaccination with a full dose increased body weight of vaccinated birds 0.2 pounds. A large proportion of broilers are vaccinated, some with a full dose, some with a half dose and some with less than a half dose. We have assumed that the average increase in body weight would be about 0.1 pound. The profit margin for broiler production is probably around 5% and represents the return after cost of feed, labor, and capital. However, for the production of the additional 0.1 pound per bird, no additional labor or capital are required. Also, feed conversion would be increased (see below) and medication would be reduced because birds would be healthier. The estimate of a 5% profit from the increased weight appears conservative. Thus, the benefits from increased efficiency of production are \$10.31 million (Table 9).

The cost of feed and labor required to produce this extra body weight was not obtained in those experiments. In other experiments (19) involving 4,000 birds, feed conversion in vaccinated birds was better than in control birds by between 0.7 and 1.5% indicating that it was less costly to feed vaccinated chickens. If half the cost of production is feed /actually cost of feed is nearer 65% of cost of production (20)/ and conversion is improved 0.25% the benefit for the years from 1972 to 1975, where the value of poultry was \$8 billion, would be \$10 million. This figure corroborates the above calculations and indicates that they are conservative. ^

5. Broiler Breeders Mortality

Losses of broiler breeders from MD have, in the past, been heavy. In one trial (7) 26.3% of broiler breeders died between 9 and 29 weeks of age from all causes whereas only 10% of a comparable vaccinated group died. Industry representatives indicate that losses from MD alone in broiler breeders from hatching to 50 weeks frequently exceed 25%; this loss is reduced to 5% by vaccination and results in reduction of 20% in MD mortality. To be conservative,

an average nationwide loss of 10% will be used for calculations. The value of broiler breeders is greater than the average value of chickens of all types and ages on farms (28, Table 563), but the latter figure is the only one available. The total benefits from vaccination of broiler breeders (Table 10) is \$16.58 million.

6. Mortality Among Pullets and Laying Egg-Type Chickens

The level of MD mortality through the life of nonvaccinated egg-laying chickens averaged 19.2% and this was reduced to 2.8% by vaccination, a difference of 16.4% (23). If application of the vaccine under general production conditions resulted in only 90% of this efficiency it would reduce the mortality in these chickens by 14.8%. Also, we estimated from discussions with industry representatives that the vaccine was used by 60% of the producers in 1971 and 90% in subsequent years. Saving from MD mortality in egg-type chickens (Table 11) is \$66.96 million.

7. Condemnations of Egg-Type Chickens

Condemnations of mature chickens, which are mostly egg-type, are given in the USDA condemnation reports (33). Once again we assume that had the vaccine not been available, condemnations would have continued at 90% of the level existing just before implementation of the vaccine, or 0.257%. The total benefits (Table 12) were \$357 thousand.

8. Benefits from Increase in Egg Production in Egg-Type Chickens

We assume again that 60% of egg producers used the vaccine in 1971 and 90% in subsequent years. Increase in egg production on a hen-day basis was between 4 and 9.3% in field trials when the vaccine was used (11, 14, 23). Also, the difference in 9 random sample tests between the eggs produced per hen housed for the 2 years before and after the institution of vaccination was 10.1% (Table 13). The number of eggs produced per chicken (28, Table 591) reached a plateau in the years from 1967 to 1970, but in 1971 the number was approximately 2% greater and from 1972 to 1973 it was 4% greater than the plateau level (Figure 1). Thus, a 2% increase for 1971 and a 4% increase thereafter was used to calculate the benefits from vaccination (Table 14), which totaled \$349.7 million.

9. Improved Feed Conversion in Egg-Type Chickens

In some studies (11), vaccinated birds required 0.12 pounds more feed per dozen eggs than unvaccinated birds; whereas, in others (14), unvaccinated birds required 0.4 pounds more feed per dozen eggs than vaccinated birds. In neither trial was there any significant effect on egg quality. Although there may be some benefits in feed conversion, they cannot be considered significant. Thus, increased egg production from vaccination probably did not decrease feed efficiency.

10. Benefits from Exploitation by Biologics Manufacturers

As indicated in Table 2, the HVT vaccine against MD was licensed for use in the state of Michigan in November 1970 and for use nationally in March

1971. There were large numbers of small producers in the states from 1970 to 1972, but no attempt has been made to estimate the vaccine produced during that time. The number of vaccine doses licensed was obtained from the Animal and Plant Health Inspection Service and the price from one of the vaccine manufacturers. These statistics are plotted in Figure 2. The number of vaccine doses licensed (10) was multiplied by the sales price, and the total dollar sales volume was obtained (Table 15). According to one manufacturer, this vaccine has yielded approximately 30% profit to the biologics manufacturers from the time the vaccine was first produced until the end of 1974. In 1975, the profit was only 20%. From this, we can conclude that biologics manufacturers made approximately \$13.17 million from the sale of the vaccine. If 50% of that profit went to Federal taxes then, approximately \$6.56 million was returned to the Federal Treasury. Approximately 50 new jobs were created in the biologics industry to produce this vaccine.

Benefits from Studies on LL

Results of work at the Regional Poultry Research Laboratory (RPRL), East Lansing, Michigan, conclusively demonstrated that lymphoid leukosis viruses (LLV's) could be transmitted from parent to offspring through the egg. This finding had great significance. In the poultry field, it threw light on the epizootiology of the disease so that attempts at eradication could be made. In the human and animal vaccine field, it indicated that vaccines propagated in avian tissues could be contaminated with egg-borne LLV's. Federal regulations now prohibit the presence of LLV's in vaccines for use in domestic animals and man. In turn, this regulation led to a demand for LLV-free eggs, which has been filled commercially. Sales of LLV-free eggs for research and biologics production exceed \$1 million; in addition, many biologics manufacturers have their own flocks of chickens. Many breeders are developing or have developed LLV-free commercial strains.

Genetic resistance to LL was discovered at the RPRL in the 1950's. The discovery was not exploited by commercial companies for many years; however, by about 1960, many companies had begun breeding programs for resistance to LL and by 1965 some progress had already been attained.

The peak of LL mortality is when the chickens are about 30 weeks of age, approximately one-quarter of the way through the laying cycle. As indicated in Table 16, the cost of producing, maintaining and feeding a laying chicken was approximately \$5.48 and the return on egg production and hen salvage was \$8.20. If the chicken died on the 30th week, then approximately one-quarter of the feed would have been eaten (\$0.75) and approximately 17.5% of the eggs would have been laid; the return for that chicken would be \$1.40. Thus, whereas the profit for healthy chickens would be \$2.72; the loss for chickens that died at 30 weeks would be \$1.83.

The benefits for breeding for genetic resistance to LL have differed greatly among the breeding companies. Some companies claim to have saved as much as 6% mortality from LL; whereas, others consider this figure too high. For the purposes of this evaluation, we assume that the saving is 1%. Thus,

from the total potential return of \$820 per 100 birds, there would be a profit of \$2.72 instead of a loss of \$1.83; i.e., a total benefit of \$4.55. Thus, the saving from a 1% decrease in LL mortality would be approximately 0.55% of the total egg production. Because other laboratories contributed to this discovery only one-half of the benefits are credited to the work at the RPRL. This amounts to \$57.87 million (Table 17).

Benefits were also realized in reduction of LL in the parent, grandparent, and great grandparents of egg-laying and broiler chickens. The value of the benefits are difficult to estimate and have not been included here.

Benefits for Human Cancer

The RNA-containing leukosis viruses and the DNA-containing MDV's have their analogs as possible causative agents of human cancer. The contribution of research at the RPRL and at the Animal Physiology and Genetics Institute, Beltsville, Maryland, has been enormous and is not measurable. For example, MD was the first cancer shown to be caused by a herpesvirus and MD is the first neoplastic condition of any animal to be controlled by a commercially applicable vaccine. Dr. Maurice Hilleman of Merck and Company (presentation at the Gustav Stern Symposium on Perspectives in Virology VIII, New York, New York--Tues., Feb. 8, 1972) recently said: "The vaccine, in my judgement, is perhaps the most outstanding development in the virus in cancer field in the last decade or two." According to Dr. Frank J. Rauscher, Scientific Director for Etiology, and now Director, National Cancer Institute: "These findings represent, through widespread acknowledgement, one of the single most important developments in cancer research within the past 10 years. These studies, which now have firmly incriminated a herpesvirus as the cause of a prevalent neoplastic disease in chickens, will contribute substantially not only to the control of this cancer in chickens but also to the prevention and control of cancers in man. The National Cancer Institute feels that these studies are so important, that field stations have been set up in the Burkitt lymphoma area of East Africa so that investigators in this country and abroad can determine the extent to which these findings are applicable to the etiology and prevention of cancers in man."

The chicken leukosis-sarcoma viruses provide one of the best understood models of virus-induced cancer. The work of ARS has contributed greatly to this understanding throughout the years. Notable examples are the demonstration of maternal transmission, genetic cellular resistance, the role of the bursa in disease, the inheritance of endogenous virus and the provision of viruses and experimental inbred chickens to other research laboratories.

Impact of Research on the Field of Science

"Citation analysis, hitherto an arcane tool of historians and sociologists of science, has now been refined to the point where it offers increasingly interesting possibilities to the science administrator. Proponents of the technique believe that within a few years it will find major uses in decisions at the level of national science policy, as an adjunct of the peer review process, and in evaluating the performance of individual scientists.

"The starting point of all citation analysis studies is to count the number of times an article or author is cited in the scientific literature. On the general assumption that the number of citations reflects an article's influence, and therefore quality, this measure can be made to serve as the fundamental yardstick for quantifying many aspects of the cognitive and social structure of science." (34)

A citation analysis was performed on the publications and scientists at the RPRL, East Lansing, and the Animal Physiology and Genetics Institute at Beltsville. The publications are listed in Appendix 2. For comparison, a laboratory in a similar field, namely, the Leukosis Experimental Unit of the Houghton Poultry Research Station, England, and a similar ARS laboratory, the Southeast Poultry Research Laboratory, Athens, Georgia, were selected. Data were already available for other ARS laboratories, the Department of Defense, state universities (26, for ARS in 1965 (29) and the Volcani Center, Institute of Soils and Water, Israel (16).

For the citation analysis, first the publications from the publications list of the laboratory were counted. The number of scientists at the laboratory each year from 1966 to 1975 was added and divided by 10 to give the average SMY per laboratory per year (Table 18). Then the number of publications per SMY was calculated. The number of times a scientist's publications was cited in the literature between those dates was obtained from Science Citation Index (12). The number of citations divided by the number of publications is the impact of the publication and indicates the average number of times each publication was cited. The number of citations divided by the number of scientists is an indication of the impact of the scientist and how many times he was cited in the literature. Because the data collected for the other laboratories represented citations in the 2 years after each publication appeared, a correction factor had to be applied to make them comparable with the above statistics which were collected for the 10-year period 1965 to 1975. This was done by comparing the percentage of total citations that occur in the 2 years after publication (an average of 20.97%) with the percentage of all the citations between these years (40.74%). We concluded that by taking all the citations between these years, approximately twice as many citations were obtained as when only 2 years after publication were taken. Thus, the figures for other authors were multiplied by 2.

The RPRL and the Animal Physiology and Genetics Institute published an average of 5.27 publications per SMY per year. This average is far greater than that of any other ARS or university laboratory tabulated. Also, the normalized impact of the publications was 2.03 citations per publication, which is higher than that of the other ARS or university laboratories except the Houghton Poultry Research Station in England, where the figures were greatly biased by one of the four scientists who had 30.83 citations per publication. Similarly, the impact of the scientists at the RPRL and the Animal Physiology and Genetics Institute was 10.73 citations per scientist, which was greater than at the other laboratories except the Houghton Poultry Research Station. Thus, where these measures are used the impact of the publications and the scientists in ARS involved in research on leukosis and Marek's disease was

greater than the impact of any of the other groups in their respective fields.

The recognition of the impact of work of the scientists at the RPRL and the Animal Physiology and Genetics Institute is in the honors and awards bestowed on the scientists. These honors and awards are listed in Appendix 3.

Summation

The benefit from ARS research on LL and MD to date is \$615 million or \$180 million for 1974 (Table 19). The first benefits went to the local vaccine producers in the different states and the first companies to use the vaccine shortly after its introduction. However, the use of the vaccine soon resulted in an over production of poultry meat and eggs which, in turn, resulted in a severe drop in prices. However, the supply and demand have now stabilized. The benefits are now derived from decrease in the cost of production of each broiler or each dozen eggs. This lower cost of production has resulted from increased efficiency and has resulted in a lower market price than would otherwise have been the case had the discoveries not been made or implemented. Thus, the consumers can purchase products at less cost than they could have without these discoveries. Producers in the industry may or may not have benefitted, depending on how rapidly they adopted the new technology. Also, the nation has benefitted because fewer resources were necessary to produce the same number of broilers and eggs as were produced before the discoveries. The natural resources, e.g., feed, can be conserved to the maximum and the human resources, e.g., labor and capital, can be diverted to other uses.

In addition to the above tangible benefits, there are many intangible benefits. They include the more predictable growout of chickens, the increase in knowledge about cancer and its application to human cancer and the impact of ARS research on other scientists in various fields, including poultry disease research and cancer research. No dollar value can be placed on these benefits, but they are undoubtedly highly significant.

The cost of the research to ARS was approximately \$15 million and the cost to the nation approximately \$31 million. The benefits of the discoveries clearly far outweigh the cost of the research.

Future Direction of Research

If we assume that the vaccine on the average is 85% effective and that 95% of the commercial poultry receive it, then the annual losses due to MD have been reduced from \$223 million by \$180 million. Thus, the current annual losses to poultry and egg production are about \$43 million. The total losses from lymphoid leukosis are approximately \$60 million annually making the losses from both diseases over \$100 million annually. Proportionately high losses are being suffered by all countries with a developed poultry industry.

Although a vaccine for Marek's disease is now available, much work still needs to be done. One of the primary problems that remain is that vaccinated

chickens, although showing no disease, are latent carriers of the potentially oncogenic field virus. This problem indicates that the vaccines, with their inherent costs and difficulties, will have to be used on a continuing basis and that the oncogenic MDV will continue to be present in a human food. There is growing evidence that herpesviruses are involved in at least 3 human neoplasms but there is no evidence that viruses causing cancer in chickens will cause disease in man. At some time in the future, we may not be allowed to use poultry containing live MDV for human food.

Possible approaches to the problem of persistent infection are development of (a) an antiviral vaccine rather than a vaccine that prevents neoplasms but has little effect on the oncogenic virus, (b) strains of chickens resistant to infection, (c) husbandry methods that make isolation rearing practical and (d) specific antiviral chemicals.

In order to increase the possibility of successful achievement of these goals, we urgently need more basic information on the virus, its multiplication in the host, the viral antigens, immunity, various types of resistance and the mechanism of tumor induction.

LL may be controlled by testing, eliminating infected breeders and rearing progeny in isolation. However, this method of eradication and isolation rearing is very costly and is in use only where infection-free eggs are required for special purposes as in vaccine production. It is not in use where eggs are produced for food. Thus, further research must be directed toward (a) development of less costly methods of detecting infection, (b) development of a practical vaccine, (c) study of genetic resistance at the level of tumor prevention and regression, (d) determination of the significance of the newly recognized E subgroup virus in the epidemiology of LL, and (e) basic studies on the immunopathogenesis of the disease, which may point to other means of controlling the disease.

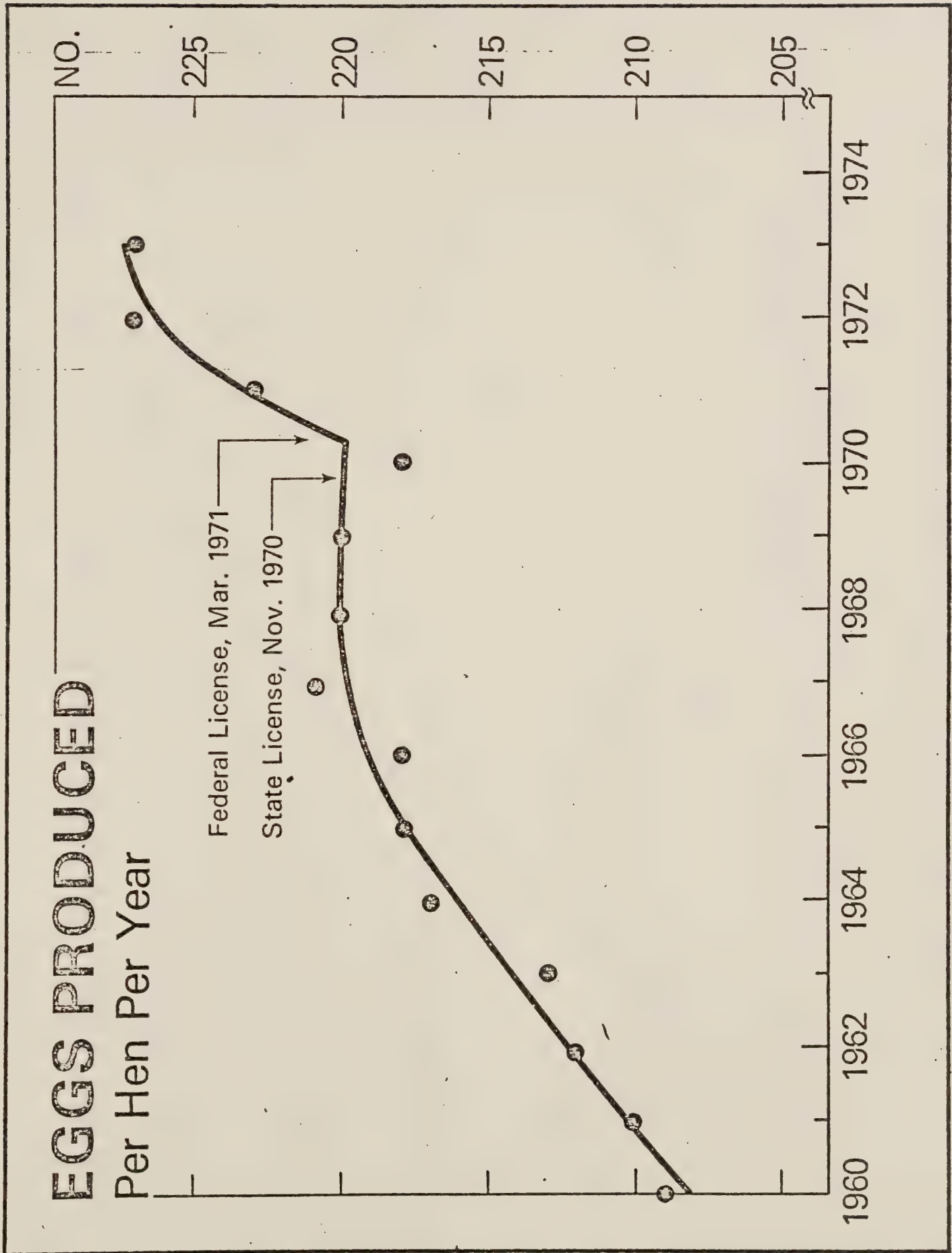
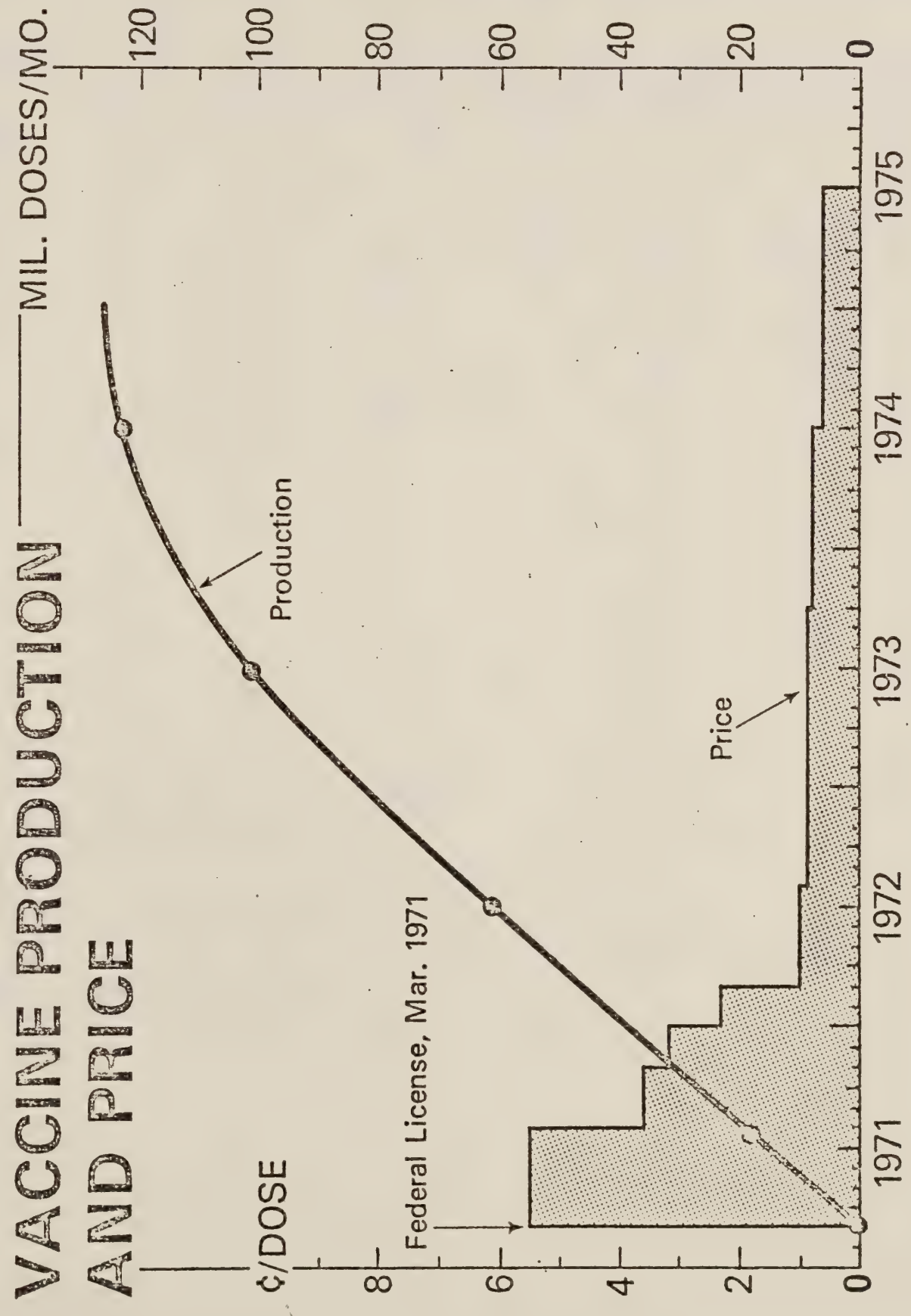
Figure 1. Rate of Lay Per Layer During the Year^a.^a From Table 591, reference 28.

Figure 2. HVT Vaccine against MD: Production and Price since Federal Licensing^a



^a From Dr. H. W. Harper, Animal & Plant Health Inspection Services and a commercial vaccine producer.

Table 1. Estimated Budget and Effort for Research
On Lymphoid Leukosis and Marek's Disease (in thousands \$)

Fiscal year	ARS ^{ab}	ARS ^b		CSRS ^{cd}	State ^d	Other ^{de}		Total	SMY ^f Effort	
		Extramural				Federal			ARS ^b	SAES ^{dg}
1966	501	30		66	177	98		872	8	10
1967	588	45		102	289	98		1,122	8	10
1968	659	115		105	319	106		1,304	10	14
1969	698	90		219	525	58		1,590	10	18
1970	879	174		277	691	133		2,154	10	25
1971	1,008	118		268	834	105		2,333	10	24
1972	1,169	0		277	1,261	110		2,817	11	30
1973	1,021	0		274	711	64		2,073	11	21
1974	986	0		306	763	90		2,145	11	17
1975	1,043	0		305	700	80		2,128	9	15
Totals	8,555	572		2,199	6,270	942		18,538	98	184

a ARS = Agricultural Research Service.

b Figures from Budget and Finance Division of ARS and include all administrative overhead.

c CSRS = Cooperative States Research Service.

d Figures from Dr. E. J. Splitter, CSRS.

e Includes research directed toward control of poultry diseases and, therefore, does not include all funds; e.g., spinoff from human cancer research. Figures are approximate.

f SMY = Scientific man-years.

g SAES = State Agricultural Experiment Stations.

Table 2. Important Chronology in Marek's Disease Research

Year	Discovery and Reference
1967	Isolation of causative herpesvirus. Churchill and Biggs ²⁴ , England. <u>Solomon et al²⁷, Mich.</u> <u>Nazerian et al¹⁷, Mich.</u>
1969	Virus production in the feather follicle. Calnek & Hitchner ³ , New York. <u>Purchase²², Mich.</u> <u>Nazerian and Witter¹⁸, Mich.</u>
1969	Protection by attenuated viruses. Churchill et al ⁶ , England.
1969	Isolation of the herpesvirus of turkeys. Kawamura et al ¹³ , Minn. <u>Witter et al³⁵, Mich.</u>
1969	Lab demonstration of protection by HVT against MD. <u>Okazaki et al²¹, Mich.</u> <u>Purchase et al²⁴, Mich.</u>
1970	Field trials of HVT vaccine. <u>Purchase et al²³, Mich.</u>
1970	Licensed by State for use in Michigan (November).
1971	Licensed by APHIS for national use (March).

Table 3. Time for Adoption of New Technology (95% Acceptance)^a

Examples	Interval	Time (years)
Vaccine for Marek's disease	1971-1973	2
Mechanical harvesting of grapes	1968-1971	3
High-yielding rice, Colombia	1967-1974	7
Hybrid corn, Iowa	1933-1940	7
Monogerm sugar beet seed	1956-1965	9
Mechanical harvesting of cherries	1961-1973	12
Hybrid sorghum	1955-1970	15
Hybrid corn, United States	1933-1969	36
High-yielding wheat, India (50 percent adoption)	1967-1973	6
High-yielding rice, Philippines (50 percent adoption)	1967-1973	6

^a From reference 36.

Table 4. Actual and Visualized Losses from Lymphoid Leukosis (LL) and Marek's Disease (MD) in Years 1965, 1975, and 1985

Kind of Losses	Nationwide Losses (%)			
	Old Technology		New Technology	
	1965 (Actual)	1975 (Visualized)	1975 (Actual)	1985 (Visualized)
1. Broilers				
Condemnation from MD	0.5 ^{ab}	1.6 ^c	0.3 ^{bd}	0.1
Condemnation from other causes	1.9 ^b	1.9	1.1 ^{bd}	0.9
Broiler mortality-MD	5.0 ^e	5.0	1.3 ^e	1.0
Reduced feed conversion (1985= 0.0)	0.5	0.5	0.2 ^f	0.0
Broiler breeder loss-LL & MD	20.0 ^g	20.0	10.0 ^g	5.0
2. Egg-Type Chickens				
Pullet mortality MD	8.9 ^h	8.9	1.3 ^h	0.5
other	5.0 ^h	5.0	2.0 ^h	2.0
Layer mortality MD	12.7 ^h	12.7	1.7 ^h	0.5
LL	5.0 ^h	4.0	4.0 ^h	0.5
other	14.0 ^h	14.0	11.0 ^h	9.0
Condemnations from leukosis	0.3 ^b	0.3	0.2 ^b	0.1
Reduced egg production (1985 = 0.0)	4.5	4.5	0.5 ⁱ	0.0

a Percentage of chickens lost or percentage of optimal performance lost at the time.

b From reference 33.

c Level existing just prior to beginning use of vaccine in 1971.

d Actual figures for 1974 from reference 33.

e From reference 31.

f From reference 9 and 19.

g From reference 7.

h From reference 23.

i From references 11, 14, and 23, Figure 1. See text.

Table 5. Leukosis Condemnations in Broilers^a

Year	Percent Condemnations	
	United States	Georgia
1961	0.11	0.08
1962	0.13	0.09
1963	0.22	0.22
1964	0.43	0.50
1965	0.52	0.54
1966	0.92	0.89
1967	1.27	1.75
1968	1.54	2.71
1969	1.48	2.54
1970	1.57	2.89
1971	1.42	2.26
1972	0.85	0.90
1973	0.47	0.26
1974	0.29	0.15

82%^b95%^b^a From reference 33.^b Reduction in condemnations from maximum in 1970.

Table 6. Benefits from Reducing Broiler Condemnations
from Marek's Disease

Year	Condemnations		Value	
	Level ^a	Reduction due to Vaccine ^b	Broilers ^c	Broilers Saved by Vaccination
	Percent	Percent	\$ Billion	\$ Million
1970	1.57			
1971	1.42			
1972	0.85	0.56	1.62	9.07
1973	0.47	0.94	2.69	25.29
1974	0.29	1.12	2.44	27.33
1975 $\frac{1}{2}$				<u>13.66^d</u>
Total to date				75.35

a From reference 33.

b Reduction in condemnations assuming that, without vaccination, losses would be at least 90% of the 1970 level, or 1.41%.

c From reference 28, Table 572 and reference 30.

d Value for half of 1975 was taken as half the value for 1974.

Table 7. Benefits from Reducing Broiler Condemnations from Other Causes by Vaccination Against Marek's Disease

Year	Condemnations		Value	
	Level ^a	Reduction ^b	Broilers ^c	Broilers Saved Vaccination ^d
	Percent	Percent	\$ Billion	\$ Million
1970	1.81			
1971	1.70			
1972	1.49	0.13	1.62	1.05
1973	1.28	0.34	2.69	4.57
1974	1.11	0.51	2.44	6.34
1975½				<u>3.17</u>
Total to Date				15.13

a From reference 33.

b Reduction in condemnations assuming that, without vaccination, losses would be at least 90% of the 1970 level, or 1.62%.

c From reference 28, Table 572 and reference 30.

d Assuming 50% reduction in other condemnations is due to vaccination against MD.

Table 8. Benefits from Reducing Broiler Mortality by Vaccination

Year	Broilers ^a		Mortality			Value	
	Hatched	Marketed	Total		Reduction ^b	Broilers ^c	Broilers Saved by Vaccine ^d
	Million	Million	Million	Percent		\$ Million	\$ Million
1969	2,846	2,702	143	5.0			
1970	2,998	2,899	98	3.3			
1971	2,976	2,863	112	3.8			
1972	3,093	2,992	101	3.3	0.3	1.62	0.49
1973	3,022	2,923	99	3.3	0.3	2.69	0.81
1974	2,954	2,917	37	1.3	2.3	2.44	5.61
1975½							2.81
Total to date							9.72

a From reference 31.

b Reduction in mortality assuming that, without vaccination, losses would be at least 90% of the average from 1969 to 1971, or 3.6%.

c From reference 28, Table 572 and reference 30.

d Assuming 10% of the reduction in mortality is due to vaccination against MD.

Table 9. Benefit from Increased Efficiency of Feed Utilization in Broilers

Year	Broilers		Value of Increased Efficiency ^c \$ Million
	Number ^a	Price/lb. ^b	
	Billions	Cents	
1972	2.99	14.1	2.10
1973	2.92	24.0	3.51
1974	2.92	21.5	3.14
1975½			<u>1.56</u>
Total to date			10.31

a From reference 31.

b From reference 28, Table 572 and reference 30.

c Value of 0.1 lb. increase in weight per broiler assuming 5% profit margin.

Table 10. Benefits from Reduction of Mortality of Broiler Breeders

Year	Broiler Breeders		Value of Breeders Saved ^c \$ Million
	Number ^a Thousands	Value ^b \$	
1972	31,108	1.28	3.98
1973	31,495	1.62	5.10
1974	29,264	1.71	5.00
1975½			<u>2.50</u>
		Total	16.58

a Number of broiler breeder chicks placed. From reference 5 and 32.

b Value per head of all chickens on the farm, excluding commercial broilers. From reference 29, Table 563 and reference 5 and 32.

c Assuming prevention of 10% loss.

Table 11. Benefits from Reducing Mortality of Egg-Type Chickens

Year	Gross Income ^a \$ Million	Percent Saved ^b by Vaccination Percent	Value of ^c Chickens Saved \$ Million
1971	95.7	14.8	8.50
1972	106.0	14.8	13.35
1973	174.1	14.8	21.94
1974	122.6	14.8	15.45
1975½			<u>7.72</u>
Total to date			66.96

a. Gross income from sale of chickens (excluding broilers).

From reference 28, Table 569.

b. Ninety percent of reduction obtained in extensive field trials.

From reference 23.

c. Approximate implementation of 60% in 1971 and 90% thereafter.

From reference 37.

Table 12. Benefits from Reducing Condemnations of Egg-Type Chickens

Year	Condemnations		Value	
	Level ^a Percent	Reduction due to Vaccination ^b Percent	Chicken ^c \$ Million	Chickens Saved by Vaccination \$ Thousand
1970	0.285			
1971	0.233	.024	95.7	23.
1972	0.188	.069	106.0	73.
1973	0.176	.081	174.1	141.
1974	0.192	.065	122.6	80.
1975 $\frac{1}{2}$				40.
Total to Date				357.

a Condemnations of mature chickens from leukosis from reference 33.

b Reduction in condemnations assuming that, without vaccination, losses would be at least 90% of the 1970 level, or 0.257%.

c From reference 28, Table 569 and reference 30.

Table 13. Benefits in Production (per hen housed) in
Random Sample Tests of Egg-Type Chickens ^a

State	Egg Production Per Hen Per Year			
	2 years before Vaccination	2 years after Vaccination	Difference	Percent
Florida	253.4	232.6	-20.8	-8.2
Minnesota	196.0	215.5	19.5	10.0
Missouri	175.1	236.3	61.2	35.0
New Hampshire	196.8	219.4	22.6	11.5
North Carolina	196.2	223.7	27.5	14.0
Pennsylvania	202.9	217.7	14.8	7.3
Tennessee	223.5	217.9	-5.6	-2.5
Canada	212.0	224.5	12.5	5.9
Missouri	196.5	232.3	35.8	<u>18.2</u>
		Average		10.1

^a From reference 25.

Table 14. Benefit from Increase in Egg Production of Egg-Type Chickens

Year	Eggs		Value of Increased Egg Production ^c
	Gross Income ^a	Increased Production after Vaccination ^b	
	\$ Billion	Percent	\$ Million
1971	1.83	2.0	21.9
1972	1.80	4.0	64.8
1973	2.91	4.0	104.8
1974	2.93	4.0	105.5
1975½			52.7
Total to date			349.7

a From reference 28, Table 591 and reference 22.

b From reference 28, Table 591 and references 11, 14, 23 and the Random Sample Tests. From reference 25.

c Assuming 60% implementation in 1971 and 90% thereafter.
From reference 37.

Table 15. Sales, Profits and Taxes of Biologics Manufacturers from Sale of the Herpesvirus of Turkeys Vaccine against Marek's Disease

Year	Sales \$ Million	Profits \$ Million	Federal Taxes \$ Million
1971	7.61	2.28	1.14
1972	8.83	2.65	1.32
1973	11.73	3.52	1.76
1974	12.44	3.73	1.86
1975½	<u>4.94</u>	<u>.99</u>	<u>.48</u>
Totals	45.55	13.17	6.56

Table 16. Cost of Growing Egg-Type Chickens

Factor	Healthy Chicken ^a Dollar	Chicken Dying of LL. Dollar
Pullet growing	1.40	1.40
Labor	.20	.20
Housing	.14	.14
Equipment	.24	.24
Other	.50	.50
Feed	<u>3.00</u>	<u>.75</u>
Total cost of producing		5.48
Eggs	8.00 ^b	1.40
Hen salvage	<u>.20</u>	<u>0.00</u>
Total receipts		<u>8.20</u>
Net profit		2.72
Net loss		1.83

a From reference 20.

b 20 dozen eggs at 40¢/doz. from reference 28, Table 591 for 1969.

Table 17. Benefit from Reducing Losses from Lymphoid Leukosis in Egg-Type Chickens

Year	Value of Eggs. ^a \$ Billion	Value of Saved Chickens and Eggs. ^b \$ Million	Benefits to Regional Poultry Lab. ^c \$ Million
1963	1.82		
1964	1.84		
1965	1.84	9.20	4.60
1966	2.16	10.80	5.40
1967	1.80	9.00	4.50
1968	1.93	9.65	4.83
1969	2.25	11.25	5.63
1970	2.22	11.10	5.55
1971	1.83	9.15	4.58
1972	1.80	9.00	4.50
1973	2.91	14.55	7.28
1974	2.93	14.65	7.33
1975½			<u>3.67</u>
Total to date			57.87

a From reference 28, Table 591 and reference 22.

b Assuming a 1% reduction in mortality which would save 0.5% of the value.

c One-half of the total benefits are ascribed to the Regional Poultry Research Laboratory.

Table 18. Impact of Research at Different Laboratories as Measured by Citations and Publications

Laboratory	Years of Study	SMY ^a	Pub per SMY ^b	Impact of Publication ^c Total	Normalized ^d	Impact of Scientist ^e Total	Normalized ^d
Regional Poultry Research Lab., East Lansing, Mich. & Physiology & Genetics Institute Beltsville, Md.	1965-75	10.6	5.27	3.03	2.03	15.96	10.73
Leukosis Experimental Unit, Houghton Poultry Research Station, Houghton, England	1965-75	4.1	4.07	9.71 ^f	3.89	39.56 ^g	15.84
ARS, Southeast Poultry Research Laboratory, Athens, Georgia	1965-75	10.6	2.67	2.36	3.53	6.30	9.43
ARS, Western Regional Research Center, Albany, Calif. ^h	1961-70	73	0.96	-	1.54 ⁱ	4.6 ⁱ	2.8 ⁱ
ARS, Eastern Regional Research Center, Wyndmoor, Pa. ^h	1961	58	2.46	-	1.74	3.8	2.6
ARS, Northern Regional Research Center, Peoria, Illinois ^h	1967	79	2.39	-	1.28	4.0	2.2
ARS, Southern Regional Research Center, New Orleans, La. ^h	1964	82	2.04	-	1.16	1.6	1.2
Department of Defense Natick Labs. ^h	1967	30	2.83	-	1.56	5.6	2.8
State Universities - sum of all departments ^{qs, h, j}	1961-68	145	2.79	-	1.70	8.4	3.8
Agricultural Research Service, USDA ^{kk}	1965	3,207	1.34	-	-	-	-
Volcani Center, ^l Inst. of Soils & Water, Israel	1959-70	37	1.67	0.73	-	1.22	-

Table 18. (Cont'd.)

- a SMY = average number of scientists per year at the laboratory.
- b Pub/SMY = publications per scientific man-year per year.
- c Average number of citations per year per publication is a measure of the impact of a publication on the field of science.
- d Total impact of publication and impact of scientist has been normalized by dividing the total impact figures by the field impact, i.e., the average citation rate of articles in the journals in which the authors from that laboratory published. For Regional Poultry Research Laboratory, the field impact was 1.49; for Houghton Poultry Research Station, 2.50; and for Southeast Poultry Research Laboratory, 0.67.
- e Average number of citations per year per scientist is a measure of the impact of the scientist in his field of science.
- f One exceptional scientist with 30.83 citations/publications.
- g One exceptional scientist with 79.29 citations/scientist.
- h From reference 26.
- i Citations are 2 years after publication. Multiplied by 2 (calculated figure 1.94) to give approximately total citations in 10 years.
- j Universities were Univ. of California, Davis, Departments of Chemistry & Food Science 1962-63); Oregon State, Department of Chemistry, Analytical (1965-69) and Organic (1965-66); Univ. of Minnesota, Department of Biochemistry (1966-67); Oklahoma State, Department of Chemistry (1963-64); Rutgers, Department of Bacteriology (1961-62); Kansas State, Department of Cereal Science (1966-67); MIT, Department Food Science & Nutrition (1967-68).
- k From reference 29.
- l From reference 16.

Table 19. Balance Sheet of Cost and Benefit from Leukosis
and Marek's Disease Research 1965-1975

Table No.	Source	Total (1965-75) Million \$	Annual (1974) Million \$
<u>Benefits from reductions in:</u>			
6	Leukosis broiler condemnations	75.35	27.33
7	Other broiler condemnations	15.13	6.34
8	Broiler mortality	9.72	5.61
9	Feed utilization	10.31	3.14
10	Broiler breeder mortality	16.58	5.00
11	Egg-type chicken mortality	66.96	15.45
12	Condemnation of egg-type chickens	0.36	0.08
14	Increased egg production	349.70	105.50
15	Profit to biologics industry	13.17	3.73
17	Reduction in lymphoid leukosis	<u>57.87</u>	<u>7.33</u>
	<u>TOTAL BENEFITS FROM RESEARCH</u>	615.15	179.51
<u>Cost of research to:</u>			
	ARS through 1965 ^a	5.93	-
1	ARS 1966-1975	8.56	1.00
1	ARS extramural	<u>0.57</u>	<u>0.00</u>
	Total cost to ARS	15.06	1.00
	Other agencies through 1965 ^a	6.11	-
1	CSRS	2.20	0.31
1	States	6.27	0.76
1	Other Federal	<u>0.94</u>	<u>0.09</u>
	Total cost to other agencies	15.52	1.16
	<u>TOTAL COST OF RESEARCH</u>	<u>30.58</u>	<u>2.16</u>

^a Estimate

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Appendix 2

The following is a list of publications from the Regional Poultry Research Laboratory obtained from the Famulus Search Program. At the end of this appendix are publications from the Animal Physiology and Genetics Institute. Original papers, exclusive of reviews, have been keyed in the right hand margin as follows:

E = Error. Publication should not have been included in printout

L = Publication of a significant discovery in lymphoid leukemia technology.

LL = Publication of a highly significant discovery in lymphoid leukemia technology.

M = Publication of a significant discovery in Marek's disease technology.

MM = Publication of a highly significant discovery in Marek's disease technology.

R = Publication of a significant discovery in Reticuloendotheliosis virus technology.

Publications have been arranged in order by author and by year.

Publications from the Animal Physiology and Genetics Institute

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F A M U L U S S E A R C H P R O G R A M

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THE DESCRIPTOR FIELD IS KEY

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190. ANONYMOUS - UNITED STATES DEPARTMENT OF AGRICULTURE, REGIONAL POULTRY RESEARCH LABORATORY 1955 LYMPHOMATOSIS IN CHICKENS U.S. DEPARTMENT OF AGRICULTURE, CIRCULAR (970), UNITED STATES GOVERNMENT PRINTING OFFICE L/S LL, REVIEW LIB-RP UNITED STATES DEPARTMENT OF AGRICULTURE, AGRICULTURAL RESEARCH SERVICE, REGIONAL POULTRY RESEARCH LABORATORY, 3606 EAST MOUNT HOPE ROAD, EAST LANSING, MI 48823 1866
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1039. BRANDLY, C.A. 1940 THE AVIAN EMBRYO. A VALUABLE AID IN DISEASE STUDY JAVMA (WAS VETERINARY MEDICINE) 35, 98-102 OTHER CHICK EMBRYO, INFECTION, CONTROL - VACCINATION, CONTROL - DISEASE LIB-RP-OK UNITED STATES DEPARTMENT OF AGRICULTURE, AGRICULTURAL RESEARCH SERVICE, REGIONAL POULTRY RESEARCH LABORATORY, 3606 EAST MOUNT HOPE ROAD, EAST LANSING, MI 48823 3002
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1168. BURMESTER, B.R. 1944 THE INFLUENCE OF CASTRATION AND THE ADMINISTRATION OF SEX HORMONES UPON THE INCIDENCE OF LYMPHOMATOSIS IN CHICKENS POSCA 23(6), 550-550 L/S, HV LL, MD, SEX, HORMONE, CONTROL - VACCINATION LIB-RP-ABSTR-OK UNITED STATES DEPARTMENT OF AGRICULTURE, AGRICULTURAL RESEARCH SERVICE, REGIONAL POULTRY RESEARCH

LABORATORY, 3606 EAST MOUNT HOPE ROAD, EAST LANSING, MI 48823 3065

1169. BURMESTER, B.R. 1945 THE INCIDENCE OF LYMPHOMATOSIS AMONG MALE AND FEMALE CHICKENS POSCA 24, 469-472 L/S LL.
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UNITED STATES DEPARTMENT OF AGRICULTURE. AGRICULTURAL RESEARCH SERVICE. REGIONAL POULTRY RESEARCH LABORATORY. 3606 EAST
MOUNT HOPE ROAD. EAST LANSING, MI 48823. PRESENT: K. NAZERIAN. UNITED STATES DEPARTMENT OF AGRICULTURE. AGRICULTURAL

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- LANSGING, MI 48823. PRESENT: B.R. BURMESTER, UNITED STATES DEPARTMENT OF AGRICULTURE, AGRICULTURAL RESEARCH SERVICE, REGIONAL POULTRY RESEARCH LABORATORY, 3606 EAST MOUNT HOPE ROAD, EAST LANSING, MI 48823 3031
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ROAD, EAST LANSING, MI 48823. PRESENT: B.R. BURMESTER, UNITED STATES DEPARTMENT OF AGRICULTURE, AGRICULTURAL RESEARCH SERVICE, REGIONAL POULTRY RESEARCH LABORATORY, 3606 EAST MOUNT HOPE ROAD, EAST LANSING, MI 48823 3021

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- 3606 E MT HOPE RD, E LANSING, MI 48823 1870
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UNITED STATES DEPARTMENT OF AGRICULTURE, AGRICULTURAL RESEARCH SERVICE, REGIONAL POULTRY RESEARCH LABORATORY, 3606 EAST
MOUNT HOPE ROAD, EAST LANSING, MI 48823 3288

472 CITATIONS SATISFY THE SEARCH REQUEST.

8681 CITATIONS WERE SEARCHED.

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END OF SEARCHING.

Honors and Awards to ARS Scientists while at the Regional Poultry Research Laboratory, East Lansing, Michigan and the Animal Physiology and Genetics Institute, Beltsville, Maryland

Regional Poultry Research Laboratory Team

- 1972 - USDA Distinguished Service Award, "for outstanding research on Marek's disease (avian leukosis) resulting in a highly efficient, safe vaccine for controlling a disease which has cost the poultry industry \$200 million annually." Presented by the Secretary of Agriculture, Earl L. Butz.

Ben Roy Burmester

- 1957 - Received Superior Service Award. Granted by the U.S. Department of Agriculture.
- 1957 - Received Borden Award. Granted by the Poultry Science Association.
- 1963 - Elected Fellow of Poultry Science Association "for distinguished services."
- 1963 - Senior Sigma Xi Award for Meritorious Research by Michigan State University Chapter.
- 1964 - Charter Diplomate, American College of Veterinary Microbiology.
- 1965 - Elected Fellow of the American Academy of Microbiology.
- 1966 - Certificate of Merit for Outstanding Performance, U.S. Department of Agriculture.
- 1970 - U.S. Department of Agriculture Superior Service Award.
- 1971 - American Poultry Hatchery Federation Award for outstanding research achievement.
- 1971 - U.S. Department of Agriculture Certificate of Merit for Outstanding performance as Director of research on the avian leukosis complex, especially Marek's disease.
- 1971 - Michigan State University College of Veterinary Medicine Alumni Award in recognition of outstanding service to the veterinary profession.

1972 - U.S. Department of Agriculture Certificate of Merit for outstanding leadership and research participation with the team which was responsible for the development of a vaccine to control Marek's disease.

1973 - Edward W. Browning Award presented by the American Society of Agronomy for outstanding achievement in the improvement of food sources anywhere in the world.

1974 - Elected Fellow of the Deutsche Akademie der Naturforscher Leopoldina.

1974 - American Feed Manufacturers Award sponsored by the American Veterinary Medical Association for leadership of a team of scientists at the Regional Poultry Research Laboratory that developed a highly effective vaccine against Marek's disease of chickens. The award consisted of a plaque and \$1,000.

1974 - Elected a "Knight of Mark Twain" by the Mark Twain Journal, Kirkwood, Missouri in recognition of outstanding contribution to Modern Medical Science, in succession to the late Sir Alexander Fleming.

1975 - U. S. Department of Agriculture Distinguished Service Award.

Lyman B. Crittenden

1965 - U.S. Department of Agriculture Incentive Award.

1965-68 - Appointment as Associate Professor, Zoology Department, Michigan State University.

Lucy F. Lee

1970 - Elected to Sigma Xi.

Keyvan Nazerian

1965 - Elected to Sigma Xi.

William Okazaki

1957 - Elected to the Society of Sigma Xi.

1970 - Best Paper Award, Avian Diseases, Plaque plus \$100 cash award.

1971 - Distinguished Service Citation and Plaque from the Michigan Allied Poultry Industries, Inc., "in recognition of outstanding service to Michigan's poultry industry."

William Okazaki (cont'd)

- 1972 - Plaque from American Poultry and Hatchery Federation-Poultry and Egg Institute of America, "in recognition for research work in the development of a Marek's disease vaccine for poultry flocks."
- 1973 - Tom Newman Memorial Award presented annually by the Poultry Stock Association of Great Britain for outstanding contribution to world poultry husbandry research reported in scientific papers during the year. The award consists of a medal and \$120 honorarium presented jointly to Dr. Purchase and Dr. Okazaki in the House of Commons, London, England.
- 1975 - Award from Japanese Science & Technology Agency for travel to Japan from June 1 through December 31, 1975.

H. Graham Purchase

- 1971 - Distinguished Service Citation and Plaque from the Michigan Allied Poultry Industries, Inc., "in recognition of outstanding service to Michigan's poultry industry."
- 1971 - Plaque from American Poultry and Hatchery Federation-Poultry and Egg Institute of America in recognition of research work in the development of a Marek's disease vaccine for poultry flocks.
- 1971 - CPC International Award of one thousand five hundred dollars, provided by the Corn Products Company, is given as an achievement award for distinctive contributions to poultry science advancement covering a period of not more than seven years preceding the annual award.
- 1972 - Arthur Fleming Award presented to the "ten most outstanding young men and women in the Federal Service."
- 1972 - Sigma Xi Junior Research Award presented by the Michigan State University Chapter for meritorious research in Microbiology.
- 1973 - Tom Newman Memorial Award presented annually by the Poultry Stock Association of Great Britain for outstanding contribution to world poultry husbandry research reported in scientific papers during the year. The award consists of a medal and \$120 honorarium presented jointly to Dr. Purchase and Dr. Okazaki in the House of Commons, London, England.

Jagdev M. Sharma

- 1968 - Elected to Phi Zeta.
- 1972 - Elected to Sigma Xi.

John J. Solomon

1959 - Member, Pi Mu Epsilon Mathematics Honorary Society

1960 - Elected to Sigma Xi

Richard L. Witter

1967 - Avian Pathology Research Award, awarded by the American Association of Avian Pathologists Research Paper Award Committee to the senior author of the paper judged best of those published in AVIAN DISEASES during 1966.

1970 - Poultry Science Association Research Award, 1971, for research judged best of that published in the area of poultry science during 1970.

1971 - Plaque from American Poultry and Hatchery Federation-Poultry and Egg Institute of America, 1971, for role in development of vaccine for Marek's disease.

1975 - Junior Research Award of the Society of Sigma Xi, Michigan State University.



